## N,N-Bis(trimethylsilyl)methoxymethylamine as a Convenient Synthetic Equivalent for +CH<sub>2</sub>NH<sub>2</sub>: N,N-Bis(trimethylsilyl)aminomethylation of Silyl Sulphides and Phosphites

## Toshiaki Morimoto,\* Masahiro Aono, and Minoru Sekiya

Shizuoka College of Pharmacy, Oshika, Shizuoka 422, Japan

N-Silyl-protected primary aminomethyl sulphides and aminomethylphosphonates can be synthesised by the Lewis acid-catalysed reactions of silyl sulphides and silyl phosphites with N,N-bis(trimethylsilyl)methoxymethylamine.

Earlier papers<sup>1,2</sup> have reported the use of N,N-bis-(trimethylsilyl)methoxymethylamine (1) as an efficient aminomethylating agent which permits the introduction of the primary aminomethyl unit not only at carbon atoms of organometallic compounds but also at the  $\alpha$ -position of carboxylic esters in a few steps. This method is of interest since the Mannich reaction is not applicable to primary aminomethylation.<sup>3</sup>

We were interested in developing a general synthesis of N-silyl-protected primary aminomethyl sulphur and phosphorus compounds by use of (1), since they should be useful synthetic intermediates. Secondary or primary amines are known to condense with formaldehyde and thiols or phosphites to afford N-mono- or N, N-bis-(sulphur or phosphorus substituted methyl)-substituted amines.<sup>4</sup> However, it is difficult to obtain N-mono-substituted amines as major products by a similar condensation using ammonia because of the formation of tertiary amines or other side products.<sup>5</sup>

The reaction of phenylthiotrimethylsilane (2a) with (1) was found to proceed in the presence of a zinc salt to yield N, N-bis(trimethylsilyl)phenylthiomethylamine (3a). The relative efficiency of the zinc salts was in the order  $ZnBr_2 > ZnCl_2 > (Et_2NCS_2)_2Zn > ZnS$ .

RSSiMe<sub>3</sub> + MeOCH<sub>2</sub>N(SiMe<sub>3</sub>)<sub>2</sub> 
$$\xrightarrow{ZnBr_2}$$
(2) (1)

RSCH<sub>2</sub>N(SiMe<sub>3</sub>)<sub>2</sub> + MeOSiMe<sub>3</sub>
(3)

In a typical experiment, a mixture of phenylthiotrimethylsilane (2a) (10 mmol), the reagent (1) (12 mmol), and

anhydrous zinc bromide (0.5 mmol) was stirred and heated at 60 °C for 3 h under nitrogen. The usual work-up and distillation gave the pure thiomethylamino compound (3a).

Table 1 shows results for the N,N-bis(trimethylsilyl)-aminomethylation of the alkylthiotrimethylsilanes (2a-d). The trimethylsilyl dithiocarbamates (2e,f) also reacted with (1) under the same conditions giving the N,N-bis(trimethylsilyl)aminomethylated products (3e,f) in high yields.

The N, N-bis(trimethylsilyl)aminomethylphosphonates (5) were obtained by the reaction of the trimethylsilyl phosphites (4) with the reagent (1) in the presence of tin(ti) chloride; the following procedure is typical. A mixture of the phosphite (4b)

**Table 1.** Reactions<sup>a</sup> of alkylthiotrimethylsilanes (2a-d) and trimethylsilyl dithiocarbamates (2e,f) with (1) in the presence of  $ZnBr_2$ .

Starting material	R	Time/h	Productb	% Yield <sup>c</sup>	B.p./°C (p/mmHg)
(2a)	Ph	3	(3a)	98	96 (0.1)
(2b)	$PhCH_2$	6	(3b)	87	120 (3)
(2c)	$Me[CH_2]_5$	35	(3c)	73	110 (6)
(2d)	EtOCOCH <sub>2</sub>	0.5	(3d)	82	111 (38)
(2e)	$Et_2NC(S)$	1	(3e)	90	d
(2f)	$[CH_2]_5NC(S)$	1	( <b>3f</b> )	94	d

<sup>a</sup> Molar ratio (2):(1):ZnBr<sub>2</sub>, 1:1.2:0.05; temp. 60 °C. <sup>b</sup> All new compounds gave satisfactory microanalytical [except (3e,f)] and n.m.r. data. <sup>c</sup> Yield of pure, isolated product [in the case of (3e,f) spectroscopically pure]. <sup>d</sup> The products (3e,f) were only slightly impure without distillation, which caused their thermal decomposition.

Table 2. Reaction<sup>a</sup> of trimethylsilyl phosphites (4) with (1) in the presence of SnCl<sub>2</sub>.

Starting material	R	Product <sup>b</sup>	% Yield <sup>c</sup>	B.p./°C (p/mmHg)
(4a)	Me	(5a)	75	115 (4.5)
(4b)	Et	(5b)	90	88 (0.1)
(4c)	Me <sub>3</sub> Si	(5c)	56	136 (15)

<sup>a</sup> Molar ratio (4):(1):SnCl<sub>2</sub>, 1:1.1:0.05; temp., 60 °C; time, 1 h. b All new compounds gave satisfactory microanalytical and n.m.r. data. c Yield of pure, isolated product.

(10 mmol), the reagent (1) (11 mmol), and anhydrous SnCl<sub>2</sub> (0.5 mmol) was stirred and heated at 60 °C for 1 h under nitrogen. Work-up gave the aminomethylphosphonate (5b).

$$(RO)_{2}POSiMe_{3} + (1) \xrightarrow{SnCl_{2}}$$

$$(4)$$

$$(RO)_{2}P(:O)CH_{2}N(SiMe_{3})_{2} + MeOSiMe_{3}$$

$$(5)$$

The mechanism of the Lewis acid catalysis may be rationalized by analogy with the previously reported reaction of epoxides or oxetanes with methylthiotrimethylsilane. The attack of a Lewis acid at oxygen of (1) would lead to an increase in the rate of electrophilic reactions of (1), leading to the formation of the thermodynamically more stable Si–O bond.

The phosphonates (5) were desilylated to give the corresponding primary amines by treatment with alcohols in a similar manner as that reported previously, 1.2 whereas the desilylation of the sulphides (3) resulted in decomposition because the desilylated species are unstable. However,

without desilylation, the *N*,*N*-bis(trimethylsilyl)aminomethyl sulphur and phosphorus compounds themselves can be regarded as synthetic equivalents of the corresponding primary amino compounds, as expected from the known reactions of *N*-silylated amines.<sup>7</sup>

Received, 16th May 1984; Com. 686

## References

- T. Morimoto, T. Takahashi, and M. Sekiya, J. Chem. Soc., Chem. Commun., 1984, 794; H. J. Bestmann and G. Wölfer, Angew. Chem., Int. Ed. Engl., 1984, 23, 53.
- 2 K. Okano, T. Morimoto, and M. Sekiya, J. Chem. Soc., Chem. Commun., 1984, 883.
- 3 M. Tramontini, Synthesis, 1973, 703.
- C. M. McLeod and G. M. Robinson, J. Chem. Soc., 1921, 119, 1470; R. R. Renshaw and D. E. Searle, J. Am. Chem. Soc., 1937, 59, 2056; G. F. Grillot, H. R. Felton, B. R. Garrett, H. Greenberg, R. Green, R. Clementi, and M. Moskowtz, ibid., 1954, 76, 3969; C. Weatherbee, R. T. Sleeter, and P. Zung-Jih Han, Tetrahedron Lett., 1965, 4069; G. F. Grillot and R. E. Schaffrath, J. Org. Chem., 1959, 24, 1035; Y. Terao, K. Matsunaga, and M. Sekiya, Chem. Pharm. Bull., 1977, 25, 2964; E. K. Fields, J. Am. Chem. Soc., 1952, 74, 1528; R. W. Ratcliffe and B. G. Christensen, Tetrahedron Lett., 1973, 4645.
- 5 I. E. Pollak and G. F. Grillot, J. Org. Chem., 1967, 32, 2891; K. A. Petrov, F. L. Maklyaev, and N. K. Bliznyuk, Zhur. Obshch. Khim., 1959, 29, 591; K. Moedritzer and R. R. Irani, J. Org. Chem., 1966, 31, 1603.
- 6 E. W. Abel and D. J. Walker, J. Chem. Soc. A, 1968, 2338.
- 7 E. W. Abel and D. A. Armitage, J. Chem. Soc., 1964, 5975; N. Duffaut and J.-P. Dupin, Bull. Soc. Chim. Fr., 1966, 3205; K. Itoh, A. Nozawa, and Y. Ishii, Tetrahedron Lett., 1969, 1421; D. A. Armitage and C. C. Tso, Chem. Commun., 1971, 1413; R. J. P. Corriu, V. Huynh, J. J. E. Moreau, and M. Pataud-Sat, Tetrahedron Lett., 1982, 23, 3257.